# APPROVED MEETING MINUTES

**California Department of Health Services, Human Stem Cell Research Advisory Committee**
**June 8, 2006**
**Stanford University**
**1:00 PM – 5:00 PM**

**Attendance:**

**California Department of Health Services (CDHS), Human Stem Cell Research (HSCR) Advisory Committee Members**
Samuel Cheshier, M.D., Ph.D.
Rabbi Elliot Dorff, Ph.D. (by phone)
Henry Greely, J.D.
Bernard Lo, M.D.
Bertram Lubin, M.D.
David Magnus, Ph.D.
Margaret McLean, Ph.D.
Radhika Rao, J.D.
Gregory Stock, Ph.D., M.B.A
Irving Weissman, M.D.

**CDHS**
Shabbir Ahmad, Manager, Human Stem Cell Research Unit, CDHS
Cindy Chambers, Human Stem Cell Research Unit, CDHS
Heidi Mergenthaler, Human Stem Cell Research Unit, CDHS
Stefanie Lee, CDHS Staff
Sandy Littlefield, CDHS Staff
Patricia Rodriguez, CDHS Legal Counsel

**Invited Guests**
Jane Lebkowski, Ph.D., Senior Vice President, Regenerative Medicine, Geron
Bryan Myers, Stanford University GCRC Representative

**Members of the Public**
Angie Boyd, Stanford University, Stanford Center for Biomedical Ethics
Mildred Cho, Stanford University, Stanford Center for Biomedical Ethics
Susan Fogel, Coordinator, Pro-Choice Alliance for Responsible Research (by phone)
Emily Galpern, Center for Genetics and Society
Kirk Klein-Schmidt, California Institute for Regenerative Medicine (CIRM)
Elizabeth Langdon-Gray, University of California, Office of the President, Office of Research
Geoffrey Lomax, Senior Officer, California Institute for Regenerative Medicine (CIRM)
Jenny McCormick, Stanford University, Stanford Center for Biomedical Ethics
Heather Richman, Stanford University, Government Relations
Shannon Smith-Crowley, ACOG, American Society for Reproductive Medicine (by phone)
Susann Steinberg, California Department of Health Services, Branch Chief, Maternal, Child & Adolescent Health/Office of Family Planning (by phone)
Terri Thorfinnson, California Department of Health Services, Chief, Office of Women's Health (by phone)
Nicole Vazquez, Senator Ortiz's Office, Senate Health Committee (by phone)

**Agenda Item #4: Approval of Meeting Minutes from February 24, 2006**

Meeting minutes from February 24, 2006 were unanimously approved.
To view the meeting minutes from February 24, 2006, see this URL:
http://www.mch.dhs.ca.gov/documents/pdf/APPROVED_HSCR_mtg_minutes_2-24-06.pdf

**Added Agenda Item: CDHS Administrative Matters**

It was requested that the Oath of Office form provided in the HSCR Advisory Committee member's packets be signed, notarized, and returned to the CDHS staff. The Oath of Office is required by the Secretary of State for every member of a statutory board or committee, without which, travel reimbursement claims will not be approved. Some HSCR Advisory Committee members also needed to sign a Conflict of Interest form. Those members that need to sign had a Conflict of Interest form provided in their packets.

**Agenda Item # 5: Discussion of SB 1260**

The main summary points of SB 1260 include:

- Removal of the sunset date of January 1, 2007 from SB 322.
- Removal of the requirement for CDHS to appoint and facilitate the HSCR Advisory Committee from SB 322.
- New regulations on oocyte procurement within the state.

Nicole Vazquez, from Senator Ortiz's office explained that the decision not to resurrect the HSCR Advisory Committee was for two reasons: the assumption that the guidelines would be completed prior to January 1, 2007, and the fiscal need to reduce costs associated with the bill. The next hearing date for the bill would most likely be either June 20 or June 27.

HSCR Advisory Committee concerns about SB 1260:

1. The guidelines created should cover pluripotent stem cells and neurogenic stem cells in addition to embryonic stem cells.
2. The removal of the HSCR Advisory Committee would not allow for external authority and validation from the scientific and ethical community as the science develops.
3. The lack of an embryonic stem cell research oversight (ESCRO) committee review for embryonic stem cell research projects in addition to the IRB review.
4. The broad language prohibiting any employee, or relative of an employee, of a "research organization" from taking part in research related to oocyte donation.
5. The expansion of medical coverage to any adverse consequences as a direct result of oocyte retrieval does not include the term "proximate"; allowing coverage for conditions that may occur many years after the procedure has taken place.

The Committee approved the motion to share their concerns with SB 1260 with Senator Ortiz and other Legislators. Dr. Lo agreed to create a draft of the Committee's concerns on SB 1260 to be approved at the end of the meeting.

**Agenda Item # 6a: Working Group Progress Reports and Committee Discussion-'Clinical Trial' Research Standards**

Dr. Magnus began the discussion by reporting on the issues that had been brought up by the working group regarding 'Clinical Trial' Research Standards.

1. Any recipients of either embryonic stem cells or materials derived from embryonic stem cells, should be informed of where the materials originated from and how they were produced.
2. The necessity of having a data safety monitoring board (DSMB) in all clinical trials and how they report their findings.

At that point, Dr. Magnus felt that the invited guest speakers would help bring some clarity to the issues the working group wanted the whole committee to consider and discuss. The first speaker, Dr. Jane Lebkowski, from Geron agreed to discuss clinical trials. Geron is working on three projects related to stem cells: spinal cord injury, differentiating cardiomyocytes for heart failure and islet cells as relates to diabetes. Currently, Geron is working on safety trials, but clinical trials for spinal cord injury may occur as soon as 14-16 months.

Dr. Lebkowski addressed these ethical issues or challenges surrounding future Geron stem cell clinical trials:

- Recipients of either embryonic stem cells or materials derived from embryonic stem cells will be informed of where the materials originated from.
- A DSMB will be involved in all clinical trials.
- Questioned the HSCR working group on why they would want a DSMB to report directly to the academic institutions, particularly if there is a conflict of interest in potentially unblinding a blinded trial.
- Informed consent forms in the early stages of clinical trials may include the language that there is an "unknown benefit" to participation in the trials instead of "no direct benefit" for participation.
- Choice of subject population will be important in clinical trials due to the dependence of variability on the clinical population looked at and the indications being looked at.
- Restrictions will be made on placement of embryonic stem cells into embryos with the intent of producing an infant child.

Questions for Dr. Lebkowski were taken from the Committee members. Dr. Weissman questioned the medical and scientific accuracy of the term 'embryo' in the statement informing the subject that they are being treated with something that has destroyed an embryo. He felt the term 'conceptus' or 'pre-implantation conceptus' would be more accurate. Dr. Stock also questioned using the language 'no personal benefit' on informed consent forms. He argued that there may be some benefit to the subject in contributing to knowledge that could eventually lead to either personal treatment or treatment for others. Dr. Lubin asked Dr. Lebkowski if the research projects were being overseen by both an ESCRO Committee and an IRB. Dr. Lebkowski responded that most of the institutions Geron works with have not heard of an ESCRO committee and that their protocols are reviewed only by an IRB. Dr. McLean questioned the safety of the stem cell lines being used by Geron in their research due to the fact that they were grown on mouse feeder cells. Dr. Lebkowski responded that the cell lines were screened for a variety of retroviruses and mouse pathogens and found to be safe. Cell lines are also karyotyped to look for abnormalities. Dr. Lebkowski ended the session by stating that uniformity in guidelines between different clinical trial sites would make coordination of multiple site trials easier to accomplish, but that sites with differing guidelines would not be overlooked if those sites could provide the infrastructure necessary for handling complicated clinical trials.

The second speaker, Bryan Myers, a representative of a general clinical research center (GCRC), spoke about issues related to DSMBs:

- Stem cell clinical trials will most likely have to be multi-site trials that are based in GCRCs throughout the country.
- DSMBs are independent of the research institution and composed of several experts in the therapy itself or the underlying disease.
- Every time the DSMB meets or an adverse event occurs, a report is made to the FDA and the IRB and CRC at the primary institution so that the study can be stopped if necessary.
- Non-NIH sponsored clinical trials can utilize the GCRC for a fee.

Dr. Magnus suggested that the guidelines should include a requirement that all clinical trials be conducted in institutions that have a GCRC. Dr. Lubin disagreed and pointed out that there are institutions without a GCRC that produce outstanding studies. Additionally, the money to support the activity of the GCRCs is questionable.

Following the presentations, Dr. Magnus continued with more issues from the working group discussions for the drafters of the guidelines to consider:

1A. Requirement for an assessment of local field strength before conducting clinical trials in human embryonic stem cell (hESC) research.
1. Re-affirm the need to adhere to all relevant regulatory requirements governing clinical trials.

Dr. Stock questioned the need for this guideline and Dr. Magnus explained that this would reiterate that the state guidelines created would not trump any federal guidelines that already exist.

2. Recipients of hESC or tissue derived from hESC are entitled to know the source of the material placed into them, including the fact that embryos may have been created or destroyed to produce the intervention under investigation.

Professor Dorff thought the language should be changed from "embryo" to "concepti". Dr. Weissman agreed that the language used should be accurate and scientific. Dr. Magnus stated that the language should be sufficient enough that the average participant in the research would be able to understand.

3. IRB determinations of when a hESC trial is ready to proceed in human populations should be based on a recommendation from an independent ESCRO committee.

Dr. Stock felt that the requirement for an ESCRO committee wouldn't always be needed if the IRB felt they had the expertise to fully evaluate a proposal. It was pointed out that all clinical trials will be reviewed by an ESCRO committee and that both the NAS guidelines and the CIRM regulations require the approval of an ESCRO committee.

4. Requirement, for safety reasons, of testing donors of biological materials before allowing clinical trials to take place.

Dr. Stock felt that the wording should include "screening" along with "testing". Dr. Magnus explained that this item was added to alert the IRBs to look for this language in the informed consent forms. Otherwise, researchers that choose to anonymize their research will not be able to use those stem cell lines later in clinical trials if they have not set up a provision for recontacting the donor for testing/screening.

5. At the present time, no hESC's should be placed into human embryos that are going to be used with the intent to create an infant.
6. All clinical trials with hESC's should be required to have a DSMB. There is some question about the reporting lines of the DSMBs.

Dr. Stock believed that like an ESCRO Committee, it may not always be necessary for a DSMB to be involved in all clinical trials. Dr. Magnus felt that the early trials should be required to have a DSMB, and this requirement may be amended at some point in the future once it becomes routine care and DSMBs are no longer needed.

7. Initial hESC clinical trials should presume no prospect of direct benefit to participants.

Professor Greely mentioned that most Phase 1 trials are conducted in healthy individuals who would not have a prospect of benefit. Dr. Stock felt that the language included in informed consent forms should be truthful about the risks and benefits involved with the research. Dr. Magnus pointed out that there are studies that are not honest about the benefits involved in participating in the research. For example, many gene transfer trials use misleading language about the prospect of benefit in the informed consent forms. Dr. Weissman believed that a researcher would not conduct research that they did not believe might have some benefit. Dr. Magnus explained that informed consent forms use the language "direct" benefit to specify the benefits of the intervention in order to distinguish between the "direct" benefit from a research trial and any indirect benefits that come about as being a participant. Dr. Lubin felt that the IRB's should be trusted to look at the informed consent forms and make decisions about whether the consent forms are protecting the subjects. The discussion was tabled so that drafters could use the discussions to develop a guideline that could be looked at in September.

8. Initial hESC clinical trials should focus on serious, life threatening diseases or chronic diseases that have a dramatic negative effect on the quality of life of participants due to the high risks of "first use in human" trials.

Dr. Stock felt that the IRBs should be making the decision about which trials to allow to continue, whether they are for serious conditions or not. Dr. Weissman agreed that putting in this recommendation may block a

line of research or therapy that does not need to be blocked. Professor Dorff felt that the risk benefit ratio in the early trials should be looked at by the IRB's. The Committee decided to drop this issue/guideline, however, this issue brought up concerns the Committee had that the IRBs may not be competent to deal with complicated hESC research issues. Professor Rao disagreed, arguing that it is not the IRBs that are incompetent but rather the current informed consent disclosures are subject to misinterpretation. Dr. Lo suggested that the Committee think carefully through the rationale behind creating a new regulatory body, such as an ESCRO Committee, to look at complicated hESC research issues.

9. Additional Committee discussion needed on whether participants in clinical trials should or should not be paid for participation.

Dr. Lubin pointed out that some IRBs permit reimbursement for time off work, and Dr. Magnus pointed out that some clinical trials have paid large amounts of money as reimbursement. The Committee decided to drop this issue/guideline as well.

10. Additional Committee discussion needed on whether IRBs should recognize research subjects and research donors as distinct categories of research participant.

Dr. Greely believed that this issue/guideline did not belong in the 'Clinical Trials' working group and it was removed from the discussion items.

**Agenda Item # 6b: Working Group Progress Reports and Committee Discussion- 'Other' Research Standards**

Professor Greely went over the issues in hESC research 'Other' than clinical trials as discussed by the second working group:

1. The guidelines should cover all pluripotent human stem cells, whether "embryonic" or not.

There is some discussion by Committee members on the definition of pluripotent. Unless certain types of pluripotent stem cells can be defined as embryonic, Dr. Rao believed that the charge of SB 322 encompasses only embryonic stem cells. Dr. Magnus felt that in order to be consistent, they should follow the language that CIRM developed for pluripotent stem cells.

2. Some parts of the CIRM regulations were not relevant to these guidelines, such as limitations on what research could be funded by CIRM. Some of the CIRM funding limitations might be reasserted as direct prohibitions.

It was agreed that because the limitations on what would not be funded by CIRM followed the NAS guidelines, these same limitations should be prohibited in the draft of the guidelines.

3. CIRM-required membership of the SCROs differed from the NAS requirements by adding a patient advocate and that the guidelines should do the same.
4. CIRM regulations broke new ground in requiring health coverage for certain side effects of the egg donation process and that the guidelines should do the same.
5. Additional Committee discussion needed about whether women who donate eggs for research purposes should receive some relatively modest payment to reimburse them partially for their time, risk and discomfort.

Professor Greely pointed out that both the NAS guidelines and the CIRM regulations ban payment for women who donate eggs for research other than for direct expenses. Dr. Stock and Professor Dorff believed that it may be difficult to acquire eggs for research if payment is not allowed, as it is for in vitro fertilization. Dr. Magnus argued that the guidelines have no choice but to follow the lead of NAS and CIRM and prohibit payments unless they can collect some empirical data showing the negative effect banning payment has on the donation of eggs for research. Any empirical data collected could then be presented to NAS and CIRM in an effort to amend current practices banning payment for oocytes. Dr. Stock believed that the researchers should be allowed to choose whether or not they want to offer payment for oocyte donation. Dr. Rao pointed out that if SB 1260 passes, it will prohibit payment for oocytes for research. Dr. Stock and Professor Dorff agreed that payment should be allowed for oocyte donors and Dr. Greely, Dr. Rao, Dr. Lo, Dr. Magnus, Dr.

Weissman, and Dr. McLean believed it should not be allowed. It was decided that the guidelines would be consistent with the NAS guidelines and CIRM regulations in prohibiting payment for oocyte donation for research.

**Agenda Item # 7: Consideration of Future Work Plan and Progress Toward Final Recommended Guidelines**

Professor Greely stated that all of the points made during the meeting will be considered by the drafters and incorporated into the guidelines. Over the summer, volunteers from the Committee will be drafting up the guidelines to be discussed at the next meeting held in the fall.

**Agenda Item # 8: Public Comment**

Susan Fogel from the Pro Choice Alliance for Responsible Research stated that her organization is opposed to women receiving payment for donation of oocytes for research because the fertility industry is not well regulated. Research on oocyte donation needs to be done and data collected on the effect that fertility drugs have on women along with the possible outcomes/side effects of these treatments. There is a concern that women of low income would be targeted and exploited for oocyte donation for research if payment was involved, and informed consent materials may not be adequate enough to explain all of the potential risks of undergoing oocyte donation.

Emily Galpern with the Center for Genetics & Society stated that California guidelines and regulations should:

- Guarantee the health and safety of all research donors as they already are for research subjects.
- Ensure that any treatments or cures that are developed from or may be developed from stem cell research in the future be widely accessible.
- Ensure diversity in research subjects for hESC clinical trials.
- Provide more input on issues related to women's health and the long term effects of oocyte donation on women.

**Added Agenda Item: Approval of Committee Draft Statement on SB 1260**

Professor Greely summarized the three major concerns with SB 1260 included in the draft document:

1. Legislation should be consistent with NAS guidelines in including requirements such as a SCRO Committee.
2. Appropriate limitations on medical care should be set for adverse consequences of oocyte retrieval.
3. Clarify and tighten restrictions on who may be a research subject.

The draft was approved by the Committee and it was also approved to allow the drafters to make editing changes before sending it on to the Legislators.

**Agenda Item # 9: Adjournment**

The Committee elected to adjourn the meeting.